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**Neuropsychological Profiles of Young Adults with High Functioning  
Autism: A Comparison to Cerebellar Cognitive Affective Syndrome**

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**Neuropsychological Profiles of Young Adults with High Functioning  
Autism: A Comparison to Cerebellar Cognitive Affective Syndrome**

**by**

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**Report**

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## **Abstract**

### **Neuropsychological Profiles of Young Adults with High Functioning Autism: A Comparison to Cerebellar Cognitive Affective Syndrome**

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The University of Texas at Austin, 2017

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Mounting evidence suggests that cerebellar dysfunction has a distinct role in the development of autism spectrum disorder (ASD; Allen, 2006, 2011; Fatemi et al., 2012). Individuals with cerebellar damage exhibit a clear pattern of neuropsychological deficits, particularly in the areas of executive functioning, language, working memory, and affect; collectively this pattern of deficits is termed cerebellar cognitive affective syndrome (CCAS) (Schmahmann & Sherman, 1998; Schmahmann, Weilburg, & Sherman, 2007). Due to the relationship the cerebellum has with both ASD and neurocognitive functioning, this study examined whether individuals with ASD exhibited the neuropsychological pattern of strengths and weaknesses characterized by CCAS.

The neuropsychological profiles of 21 adult males with high functioning autism spectrum disorder (HFASD) were compared to 22 matched healthy controls. The groups were compared using independent samples t tests. We found that the HFASD group performed worse on most neuropsychological measures; however significant differences were only found on speeded motor tasks. Such findings suggest that the heterogeneity of the HFASD group may mask the expected patterns of strengths and weaknesses that are similar to CCAS.

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## **Literature Review**

### **AUTISM SPECTRUM DISORDER**

Autism spectrum disorder (ASD) is a neurodevelopmental disorder exemplified by restrictive, repetitive behavior and deficits in social communication (American Psychiatric Association [APA], 2013). ASD affects 1% of the U.S. population and is diagnosed in approximately 1 out of every 68 children (APA, 2013; Baio, 2014). The prevalence of ASD is growing each year, especially in populations of youth with average intelligence (APA, 2013; Baio, 2014). The DSM-5 does not officially delineate the diagnostic term of “high-functioning autism spectrum disorder” (HFASD); however, this is a useful clinical expression that characterizes individuals with average intelligence who have been diagnosed with ASD. Forty-six percent of children diagnosed with ASD have an IQ>85 (Baio, 2014).

### **AUTISM SPECTRUM DISORDER AND THE CEREBELLUM**

The cerebellum is at the forefront of an increasing body of research examining its contribution to the development of autism. Evidence for the involvement of the cerebellum in autism can be found in several different areas of research, including investigations regarding cerebellar damage during development (Wang et al., 2014), anatomical and imaging studies (Allen, 2006, 2011; Bauman & Kemper, 1994; Courchesne et al., 1994; Khan et al., 2015), genetic disorders involving the cerebellum (Fatemi et al., 2012), and the presence of motor and cognitive deficits associated with cerebellar function (Freitag, Kleser, Schneider, & Gontard, 2006).

Autism is a neurodevelopmental disorder, and damage to the cerebellum during development has been linked to ASD symptomology (Fatemi et al., 2012). Damage to the cerebellum during sensitive time periods in development increases the risk for autism 36-



fold (Wang et al., 2014). Additionally, cerebellar damage at birth produces social deficits similar to those seen in ASD and is correlated with high scores on autism screening inventories (Limperopoulos et al., 2007). These studies suggest that cerebellar damage and dysfunction can be crucial antecedents to the development of autistic symptoms.

Anatomical cerebellar abnormalities are present in early life and persist into adulthood, providing consistent and compelling evidence for the role of the cerebellum in the development of autism (Wang et al., 2014). When children with autism are as young as two years, defects are often seen in the cerebellar vermis, while in the cerebellar hemispheres there are increases in white matter compared to gray matter (Courchesne et al., 1994; Wang et al., 2014). Postmortem studies indicate that there is a reduction of Purkinje cells in the posterolateral neocerebellar cortex and archicerebellar cortex of the cerebellar hemispheres in most individuals with autism (Allen, 2006; Bauman & Kemper, 1994; Whitney, Kemper, Bauman, Rosene, & Blatt, 2008). Researchers have also found that some children with ASD have large and plentiful cerebellar neurons, but older adults with ASD have smaller and fewer neurons in the cerebellum (Kemper & Bauman, 1998). Finally, in terms of functional connectivity between the cerebellum and cerebral cortex, many individuals with ASD have hyperconnectivity between the cerebellum and sensorimotor areas of the cerebral cortex, but reduced connectivity between the cerebellum and supramodal (e.g. prefrontal, posterior parietal) areas of the brain (Khan et al., 2015). Distinct anatomical differences in the cerebellum of individuals with ASD highlight the cerebellum's role in autism.

Many genetic disorders also produce autism-like symptomology; a comorbid ASD diagnosis is more likely when there are dysfunctions in the cerebellum. Imaging studies show differences in the cerebellar vermis lobules VI-VII in individuals with fragile X syndrome who are diagnosed with ASD versus individuals without the ASD diagnosis

(Fatemi et al., 2012). Likewise, individuals diagnosed with Tuberous sclerosis who had more severe autism symptomology were shown to have more lesions in the cerebellum (Eluvathingal et al., 2006). Finally, Joubert syndrome is characterized by cerebellar hypoplasia and about 40% of individuals with Joubert syndrome are also diagnosed with ASD (Fatemi et al., 2012). Taken together, more severe impairment of the cerebellum in certain genetic disorders is associated with more severe autism symptomology.

Motor deficits characterized by cerebellar dysfunction provide further evidence that the cerebellum plays a key role in autism symptomology. Multisensory deficits and deficits in the areas of pointing, balancing, and timing in individuals with autism suggest cerebellar involvement in the disorder (Freitag et al., 2006; Gowen & Miall, 2005). Imaging studies further support the cerebellar influence on motor and cognitive tasks; individuals with ASD have increased activation of the cerebellum during motor tasks compared to healthy control subjects, and decreased cerebellar activation during cognitive tasks relative to controls (Allen & Courchesne, 2003; Allen, Müller, & Courchesne, 2004). There is ample evidence of the involvement of the cerebellum in the development of ASD.

#### **THE CEREBELLUM, NEUROPSYCHOLOGICAL FUNCTIONING, AND CEREBELLAR COGNITIVE AFFECTIVE SYNDROME**

The cerebellum has traditionally been associated with motor control and coordination, but in the last few decades, there has been a shift in the literature connecting the cerebellum with higher cognitive functioning (O'Halloran, Kinsella, & Storey, 2012; Strick, Dum, & Fiez, 2009; Tedesco et al., 2011). Evidence for a cerebellar role in cognitive functioning is supported through neuroanatomical studies, neuroimaging studies, and studies of individuals with cerebellar pathologies.

Meta-analyses suggest that there is a topographic organization of the cerebellum during higher cognitive functioning and that cerebellar activation is evident during a

variety of cognitive tasks, such as executive functioning, language, working memory, and visuospatial tasks (Keren-Happuch, Chen, Ho, & Desmond, 2014; Stoodley, 2012; Stoodley & Schmahmann, 2009). Results from functional connectivity magnetic resonance imaging (fcMRI) provide evidence that there are functional connections between the cerebellum and the prefrontal cortex in humans; the cerebellum contributes to motor and cognitive functioning through reciprocal connections with the prefrontal cortex, posterior parietal cortex, and cortical motor regions (Allen et al., 2005; Strick et al., 2009).

There are anatomical links between neuropsychological deficits observed and specific areas of the cerebellum. Deficits in cognitive areas have been anatomically linked to the posterior lobe of the cerebellum (Schmahmann & Sherman, 1998; Sundberg & Sahin, 2015; Tavano et al., 2007). Deficits in executive functioning, visuospatial abilities, and linguistic abilities have been linked to cerebellar hemispheres (Schmahmann & Sherman, 1998; Sundberg & Sahin, 2015; Tavano et al., 2007; Tedesco et al., 2011). In contrast with these areas of higher order functioning, affective and emotional disturbances have been associated with impairments in the cerebellar vermis (Schmahmann & Sherman, 1998; Sundberg & Sahin, 2015; Tavano et al., 2007; Tedesco et al., 2011).

Cerebellar cognitive affective syndrome (CCAS) was a term presented by Schmahmann and Sherman in 1998 to collectively describe the pattern of deficits observed in individuals with cerebellar damage. Much of the research detailing the role of the cerebellum in higher order functioning has been generated from studies of patients with cerebellar damage (O'Halloran et al., 2012; Schmahmann & Sherman, 1998). Researchers consistently demonstrate that patients with cerebellar damage exhibit deficits in visuospatial functioning, language, executive functions, mood, and affect (O'Halloran et al., 2012; Schmahmann & Sherman, 1998; Tedesco et al., 2011). In their pioneering article, Schmahmann and Sherman conducted neurological examinations, bedside mental state

tests, neuropsychological assessments, and neuroimaging on 20 patients with cerebellar diseases. Patients with lesions in the posterior lobe of the cerebellum and vermis exhibited prominent behavioral changes as well as impairments in executive functioning (e.g. planning, set shifting, verbal fluency), visual spatial organization, language deficits (e.g. aggrammatism, dysprosodia), and personality change (e.g. blunted affect, disinhibited behavior) (Schmahmann & Sherman, 1998). Patients with lesions in the anterior lobe of the cerebellum had minor changes in executive functioning and visual spatial abilities (Schmahmann & Sherman, 1998).

CCAS has been described in many different populations. A developmental form of CCAS has been demonstrated through metanalysis in individuals who survived cerebellar injury in their infancy (Brossard-Racine, Plessis, & Limperopoulos, 2014), it has been described in individuals with Machado Joseph disease (Braga-Neto et al., 2011), and it has been discovered in child survivors of cerebellar tumors (Levisohn, Cronin-Golomb, & Schmahmann, 2000). Despite the widespread use of the term CCAS, there is some concern about the guidelines for diagnosing CCAS, considering not all patients exhibit all of the core features of the syndrome (Omar et al., 2014).

## **AUTISM AND NEUROPSYCHOLOGICAL FUNCTIONING**

The most consistent findings in studies examining the full neuropsychological profiles of individuals with HFASD compared to healthy controls include impairments in executive functioning, memory, and language abilities (Williams, Goldstein, & Minshew, 2006). In a comparison of children with high functioning autism and healthy controls on a complete neuropsychological evaluation utilizing the NEPSY-II, researchers found that participants with HFASD demonstrated deficits in attention, executive functioning, language, learning and memory, and sensorimotor abilities compared to the control

subjects (Narzisi, Muratori, Calderoni, Fabbro, & Urgesi, 2013). A similar analysis conducted by Barron-Linnankoski and colleagues found weaknesses in set-shifting, verbal fluency, and narrative memory on the NEPSY-II in children with HFASD compared to controls (Barron-Linnankoski et al., 2015). An additional study comparing children with HFASD and controls on the NEPSY found that individuals with HFASD performed significantly worse on 8 of the 14 subtests after controlling for IQ (Hooper, Poon, Marcus, & Fine, 2006). When comparing 27 adults with Asperger's syndrome to 20 healthy controls, researchers found that individuals with Asperger's syndrome performed significantly worse on measures of visual memory and on executive functioning tasks involving flexibility and generativity (Ambery, Russell, Perry, Morris, & Murphy, 2006).

Most research regarding adults with HFASD focus on single areas of neuropsychological functioning and do not provide outcomes regarding the full neuropsychological profile for individuals with HFASD. Investigators that have examined the full neuropsychological profiles of individuals with ASD focus on children (e.g., Barron-Linnankoski et al., 2015; Narzisi et al., 2013), compare individuals with HFASD and Asperger's without a typically developing control (e.g., Meyer & Minshew, 2002), or do not adequately control for Type I error (Ambery et al., 2006). Additionally, most researchers focus on a broad range of intellectual functioning, while evidence suggests that intellectual functioning moderates neuropsychological functioning in individuals with ASD; individuals with ASD with higher IQs experience greater relative neuropsychological deficits compared to individuals with ASD who have low IQs (Rommelse et al., 2015). Altogether, there is a need for a more nuanced understanding of the the full pattern of strengths and weaknesses in the neuropsychological profiles of adults with HFASD compared to matched typically developing controls within a similar range of intellectual functioning.

## **PRESENT STUDY: AUTISM AND CEREBELLAR COGNITIVE AFFECTIVE SYNDROME**

The current research study examines whether the neuropsychological profiles of adults with HFASD differ significantly from a group of matched healthy controls. Additionally, we examine whether the HFASD group exhibits a similar pattern of weaknesses seen in the profiles of patients with CCAS. Due to the role of the cerebellum in ASD, we hypothesize that the neuropsychological profile of adults with HFASD will be similar to the neuropsychological profile of individuals with cerebellar damage. Specifically, we hypothesize that individuals with HFASD will have lower performance on measures of executive functioning, memory, and motor skills compared to matched healthy controls.

## **Method**

Data were previously collected as part of a larger study examining the anatomical and functional connectivity of the cerebellum in ASD. All data were deidentified prior to the current study.

### **PARTICIPANTS**

Twenty-one adult males with a diagnosis of ASD were recruited into the study via professional recommendation and self-referral as well as advertising through various agencies, conferences, schools, and websites. Inclusion criteria were: (a) 18 to 26 years-old; (b) English as primary language; (c) diagnosed with autism spectrum disorder. Exclusion criteria were: (a) IQ<80; (b) known history of epilepsy, mental retardation, fragile X syndrome, or other psychiatric or neurologic diagnosis; (c) head injury that involved loss of consciousness for more than 30 minutes; (d) any significant physical or psychiatric disability that prevented involvement in the study.

Prior to continuation in the study, participants in the ASD group were assessed by a psychologist with expertise in diagnosing autism. The Autism Diagnostic Interview-Revised (ADI-R; Lord & Rutter, 1994) and the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1989) were administered to confirm ASD diagnosis using DSM-IV diagnostic criteria (APA, 2000).

The neuropsychological performance of the participants with HFASD was compared to 22 healthy controls matched by gender, age, and Performance IQ. Prior to continuation in the study, participants in the healthy control group were screened using the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). Participants determined to be a good match were subsequently enrolled into the study to complete further testing.

Baseline age and intellectual functioning for individuals in both groups is described in Table 1. Two participants in the HFASD group were left-handed and 3 participants in the control group were left-handed.

Table 1: Age and IQ for individuals in the HFASD and Control groups.

	HFASD		Control	
	M	SD	M	SD
Age	20.988	2.139	21.421	2.305
Full IQ	118.905	11.532	120.773	11.6616
Verbal IQ	115.381	15.062	118.818	13.2292
Performance IQ	118.475	9.212	118.091	10.7699

All IQ scores are standard scores with a mean (M) of 100 and standard deviation (SD) of 15

## NEUROPSYCHOLOGICAL EVALUATION

All subjects gave informed consent prior to testing, and were compensated for their time. The University of Texas at Austin Institutional Review Board approved all procedures. All participants underwent a full neuropsychological evaluation, conducted by a trained administrator. The tests selected to be part of this neuropsychological assessment battery were chosen to replicate previous evaluations in the study of CCAS. Participants were assessed across six separate domains: executive functioning, visuospatial ability, language, learning and memory, attention, and motor speed. Psychometric information for the selected neuropsychological measures is provided in Appendix A.

### Intellectual functioning

The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was administered as a screening measure for intelligence. The WASI consists of four subtests:



Vocabulary, Block Design, Similarities, and Matrix reasoning. The WASI provides a Full IQ score, a Verbal IQ score, and a Performance IQ score.

### **Executive functioning**

Wisconsin Card Sorting Test. The Wisconsin Card Sorting Test (WCST; Heaton & PAR Staff, 2003) is considered a “gold standard” measure of executive functioning; specifically, it measures abstract reasoning and cognitive set-shifting (Ozonoff, Goodlin-Jones, & Solomon, 2005). On the computerized version, participants matched response cards to one of four stimulus cards and determined the correct sorting principle; after ten correct responses the sorting principle changed. The score for perseverative responses was used in the analysis.

Trail Making Test. The Trail Making Test (TMT; Strauss, Sherman, & Spreen, 2006) is one of the most commonly used neuropsychological tests for executive functioning; it measures cognitive flexibility, set-shifting, and sequencing abilities. During the Trails B task, participants were asked to alternatively sequence letters and numbers (e.g. 1-A, A-2, 2-B, B-3, 3-C, etc.). Trails B is scored based on the time taken to complete the task.

Verbal Fluency. For the verbal fluency tasks (Strauss et al., 2006), participants were asked to provide as many words as possible that began with the specified prompt for one minute. In the Controlled Oral Word Association test (COWA), a measure of phonemic fluency, participants were asked to name as many words as they could that began with a certain letter (i.e. F, A, S). On the category fluency task, a measure of semantic fluency, participants were asked to name as many words as they could that belonged to a particular category (i.e., animals). Total scores for phonemic and semantic fluency are based on the number of unique, admissible words.

## **Visuospatial ability**

Judgment of Line Orientation. Judgment of Line Orientation (JLO; Benton, Sivan, Hamsher, Varney, & Spreen, 1994) measures spatial perception and orientation. The JLO consists of a stimulus book and multiple choice answers; participants were asked to select a pair of lines from the multiple choice options that best matched a pair of angled partial lines. The JLO total score is the number of correct responses.

## **Language**

Boston Naming Test. The Boston Naming Test-2 (BNT-2; Kaplan, Goodglass, & Weintraub, 2001) is a measure of visual naming ability. Participants were asked to name 60 pictures that were presented to them; if they provided an answer that was a misinterpretation of the picture they were provided a stimulus cue. The total number correct is the number of spontaneously correct answers added to the number of correct responses after stimulus cues are provided.

Peabody Picture Vocabulary Test. The Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4; Dunn & Dunn, 2007) is a measure of receptive English language. Participants were asked to point to a picture on the stimulus book that corresponded with a word the examiner read. The PPVT is scored based on the total number of correct responses.

## **Learning and memory**

Brief Visuospatial Memory Test. The Brief Visuospatial Memory Test-Revised (BVMT-R; Benedict, 1997) is a measure of visual learning and assesses visuospatial judgment, spatial orientation, and spatial perception. Participants were presented with a stimulus composed of six figures and were asked to study the figures for 10 seconds. The participants were then asked to draw as many figures as they could remember. This process

was repeated two more times with the same figures for a total of three trials. Each figure was scored based on location and accuracy. Total scores were based on the number of words remembered across all three trials. Total score for immediate recall was used for this analysis.

**Hopkins Verbal Learning Test.** The Hopkins Verbal Learning Test-Revised (HVLT-R; Brandt & Benedict, 2001) is a list learning task and is a measure of verbal learning and memory. Participants were read a list of twelve words and were asked to remember the list across three trials. Total scores were based on the number of words remembered across all three trials. Total score for immediate recall was used for this analysis.

### **Attention**

**Conners' Continuous Performance Test.** The Conners' Continuous Performance Test, Second Edition (CPT-II; Conners & MHS Staff, 2000) is a computerized test that measures sustained attention and response inhibition. Participants were asked to press the spacebar every time a letter was presented on the screen, except when they saw the letter "X." The score generated for omission errors (no response after a non-letter x) was selected for this analysis.

**Digit Span Forward.** Digit Span Forward is one of the working memory subtests from the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV; Wechsler, 2008) and is a measure of elementary attention. In this task, participants were provided a list of numbers that they were asked to hold in awareness and immediately repeat. A standard score was derived from the number of correct responses.

## **Motor Functioning**

Lafayette Grooved Pegboard. Fine motor skills were examined using the Lafayette Grooved Pegboard (Matthews & Klove, 1964). The Grooved Pegboard test requires complex visual-motor coordination and measures manual dexterity. In this assessment, participants were asked to pick up and rotate pegs to place them in randomly positioned keyholes in the pegboard. Scores were derived from completion time for the dominant and non-dominant hand.

## **ANALYSIS**

SPSS statistical software package version 22.0 was used for all statistical analyses. All raw scores were converted to standard scores based on available test norms; all standard scores were converted to z-scores for the purposes of the analysis and some scores were transformed so that higher scores represented better functioning. Two-tailed independent samples t tests were performed to determine which neuropsychological tests were significantly different between groups. Cohen's d was calculated to reflect an estimate of the effect sizes. For the independent samples t tests, the Bonferroni-Holm (1979) correction was used to control the error rate for multiple comparisons to keep the overall alpha < .05.

## Results

Table 2: Comparison of performance on neuropsychological tasks between HFASD and Control groups

	HFASD		Control					
	M	SD	M	SD	t	df	P1	d
<b>Executive Functioning</b>								
WCST	-0.379	0.998	-0.294	0.991	-0.256	33.6	0.800	-0.09
Trails B	-1.316	1.827	-0.098	1.206	-2.550	34.6	0.015	-0.87
Semantic Fluency	-0.288	1.321	0.565	1.010	-2.331	35.5	0.026	-0.78
Phonemic Fluency	-0.031	1.028	0.330	0.792	-1.287	37.6	0.206	-0.42
<b>Visuospatial Ability</b>								
JLO	0.289	0.635	-0.060	0.895	1.408	34.3	0.168	0.48
<b>Language</b>								
BNT	-0.524	1.100	-0.501	1.361	-0.057	34.7	0.955	-0.02
PPVT	0.830	1.157	0.983	.954	-0.457	36.7	0.650	-0.15
<b>Learning and Memory</b>								
BVMT	-0.706	1.355	-0.305	1.203	-0.997	36.4	0.325	-0.33
HVLT	-0.533	1.486	-0.396	0.983	-0.357	34.5	0.723	-0.12
<b>Attention</b>								
CPT	0.429	0.732	0.170	0.832	0.974	31.9	0.337	0.34
Digit Span	-0.318	1.218	0.561	0.701	-2.880	31.6	0.007	-1.02
<b>Motor Functioning</b>								
Dominant Hand	-1.530	1.286	-0.422	0.955	-3.144	36.9	0.003*	-1.04
Nondominant Hand	-1.707	1.557	-0.476	0.726	-3.267	28.6	0.003*	-1.22

d, Cohen's d; All scores are z-scores with a mean (M) of 0 and standard deviation (SD) of 1;

p 1=Unadjusted p values; \* = $P < .05$ , significant after Bonferroni-Holm correction

An initial comparison revealed no significant difference between the groups on Full IQ [ $t(41) = -0.528$ ,  $p=0.600$ ], Performance IQ [ $t(41) = 0.126$ ,  $p=0.901$ ], or Verbal IQ [ $t(41) = -0.796$ ,  $p=0.431$ ]. Additionally, the groups did not differ on age [ $t(41) = -0.764$ ,  $p=0.449$ ] or handedness. The groups were evenly matched on all key variables, therefore we did not control for IQ or age [see Dennis et al., (2009) for further arguments against controlling for IQ]. A description of the results for each neuropsychological domain is

described below and displayed in Table 2. All results reported assume unequal variances between the groups.

## EXECUTIVE FUNCTIONING

The HFASD group scored moderately lower than the control group on all measures of executive functioning examined. Differences between the two groups approached significance on the Trails B [ $t(34.6) = -2.550, p=0.015, d= -0.87$ ] and semantic fluency [ $t(35.5) = -2.331, p=0.026, d= -0.78$ ] measures; however, they did not reach the appropriate significance level after adjusting for multiple comparisons using the Bonferroni-Holm correction. Differences between the two groups were not significant for the WCST or the phonemic fluency task. See Figure 1 for a bar graph comparing the group means.

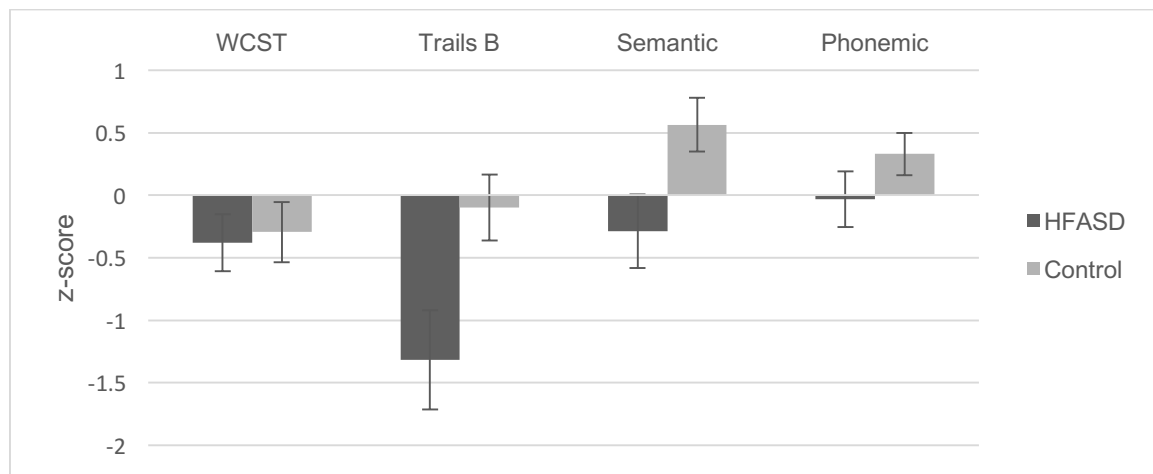


Figure 1: Executive functioning group means

This figure illustrates the mean scores of the HFASD (high functioning autism spectrum disorder) group (dark grey) and the control group (light grey) on the four measures of executive functioning: the Wisconsin Card Sorting Test (WCST), Trails B, semantic fluency (Semantic) and phonemic fluency (Phonemic). The bars represent standard errors.

## VISUOSPATIAL ABILITY

On the Judgment of Line Orientation test, the HFASD group scored moderately higher than the control group, but the groups did not differ significantly. See Figure 2 for a bar graph comparing the group means.

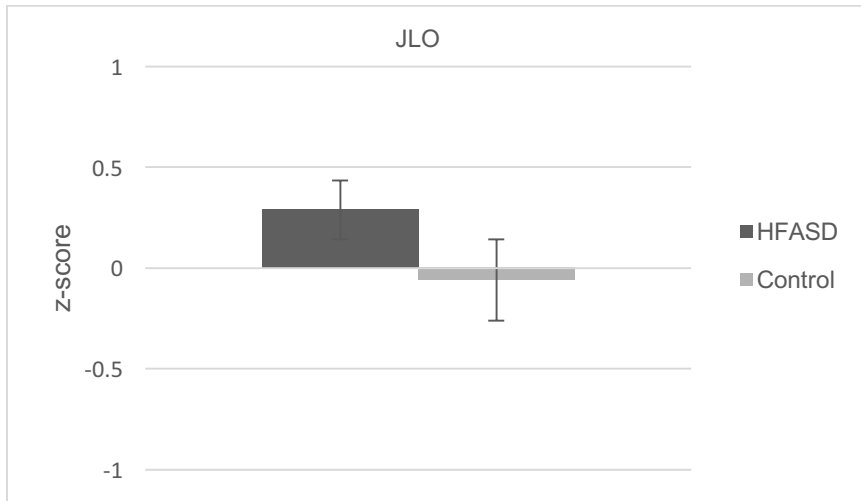


Figure 2: Visuospatial ability group means

This figure illustrates the mean scores of the HFASD (high functioning autism spectrum disorder) group (dark grey) and the control group (light grey) on the Judgment of Line Orientation task (JLO). The bars represent standard errors.

## LANGUAGE

On measures of expressive and receptive language, the HFASD group did not differ significantly from the control group. See Figure 3 for a bar graph comparing the group means.

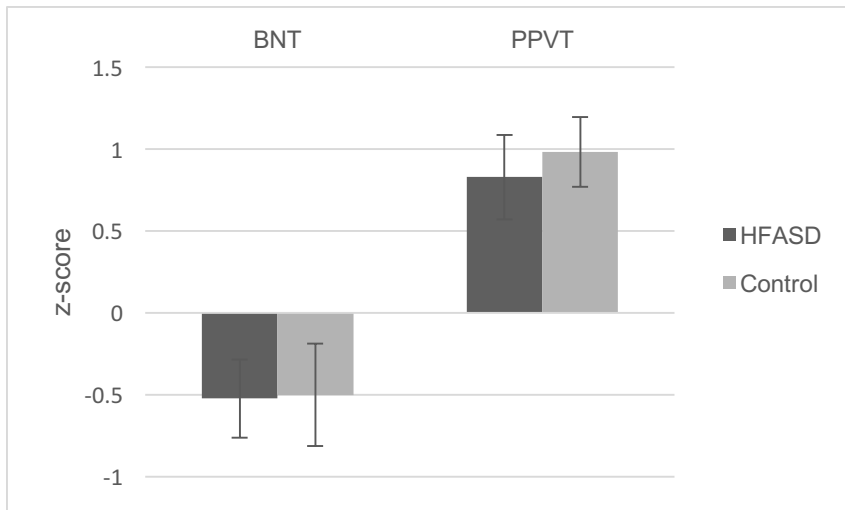


Figure 3: Language group means

This figure illustrates the mean scores of the HFASD (high functioning autism spectrum disorder) group (dark grey) and the control group (light grey) on the two measures of language: the Boston Naming Test (BNT) and the Peabody Picture Vocabulary Test (PPVT). The bars represent standard errors.

### LEARNING AND MEMORY

On the BVMT and HVLT, the HFASD group did not differ significantly from the control group. See Figure 4 for a bar graph comparing the group means.



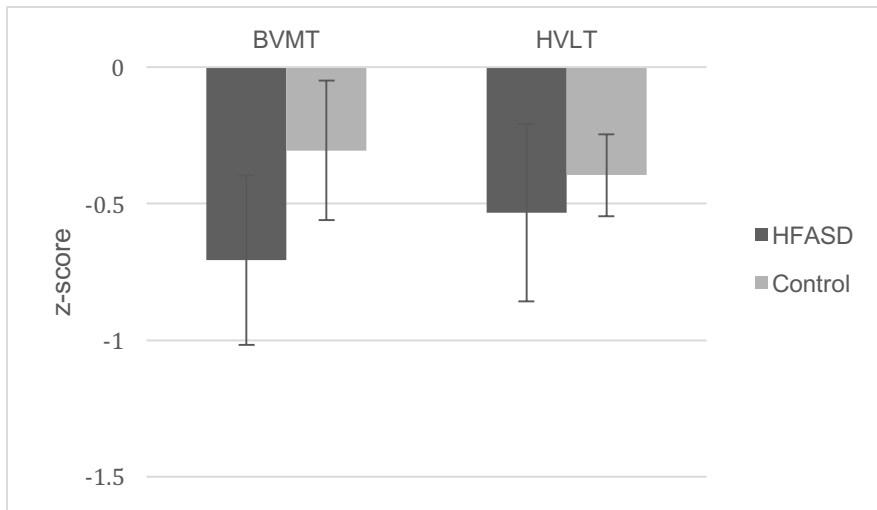


Figure 4: Learning and memory group means

This figure illustrates the mean scores of the HFASD (high functioning autism spectrum disorder) group (dark grey) and the control group (light grey) on the two measures of learning and memory: the Brief Visuospatial Memory Test (BVMT) and the Hopkins Verbal Learning Test (HVLt). The bars represent standard errors.

## ATTENTION

Performance of the HFASD group varied on measures of attention. On the digit span forward task, individuals in the HFASD group performed slightly worse than the control group. Differences between the groups approached significance [ $t(31.6) = -2.880$ ,  $p=0.007$ ,  $d=-1.02$ ]; however, they did not reach the appropriate significance level after adjusting for multiple comparisons using the Bonferroni-Holm correction. In contrast, the HFASD group had slightly better performance than the control group on the CPT; however, this difference was not significant. See Figure 5 for a bar graph comparing the group means.

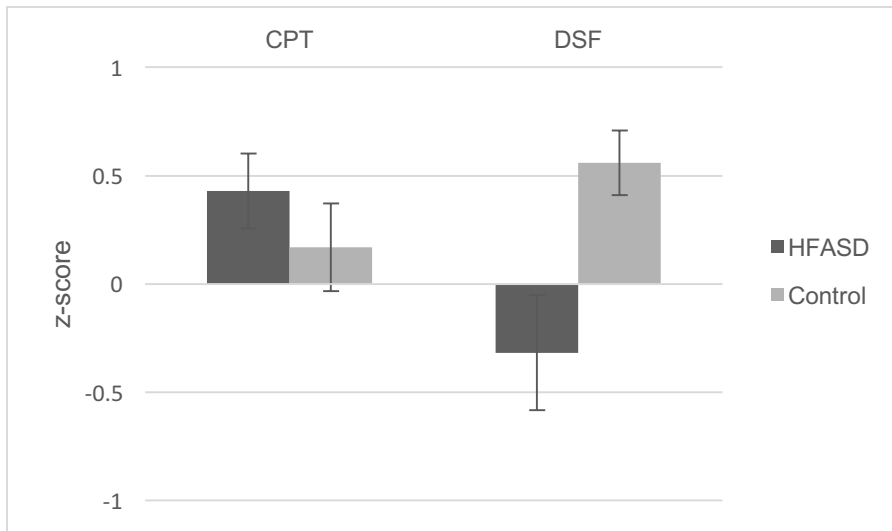


Figure 5: Attention group means

This figure illustrates the mean scores of the HFASD (high functioning autism spectrum disorder) group (dark grey) and the control group (light grey) on the two measures of attention: the Conner's Continuous Performance Test (CPT) and the Digit Span Forward subtest (DSF). The bars represent standard errors.

### MOTOR FUNCTIONING

On the grooved pegboard test, the HFASD group performed significantly worse than the control group for both their dominant [ $t(36.9) = -3.144, p=0.003, d= -1.04$ ] and nondominant [ $t(28.6) = -3.267, p=0.003, d= -1.22$ ] hands. Performance of the HFASD group was a full standard deviation below the control group on both hands, and the calculated effect size was large. See Figure 6 for a bar graph comparing the group means.

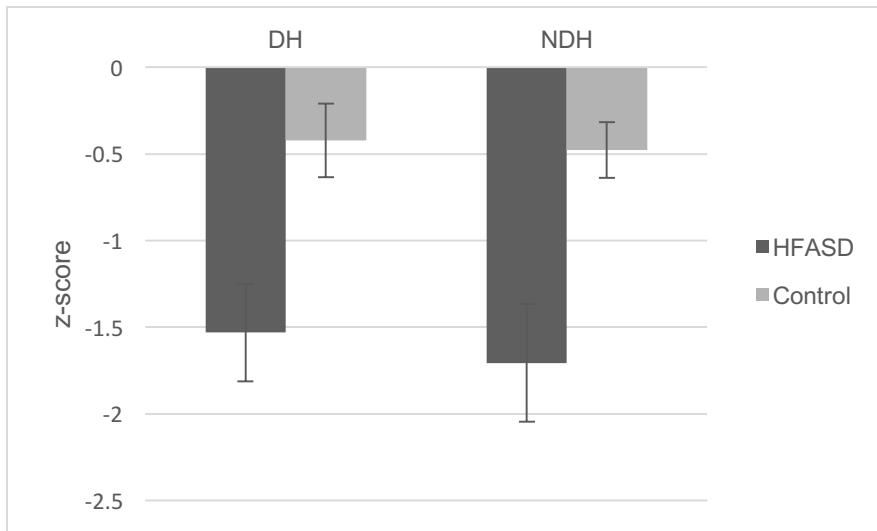


Figure 6: Motor speed group means

This figure illustrates the mean scores of the HFASD (high functioning autism spectrum disorder) group (dark grey) and the control group (light grey) on the grooved pegboard test for dominant hand (DH) and nondominant hand (NDH). The bars represent standard errors.

## **Discussion and Conclusions**

Research suggests that individuals with ASD exhibit similar patterns of deficits as individuals with CCAS; however, no study to date has examined the neuropsychological profiles of individuals with HFASD to determine if they follow the pattern of weaknesses seen in CCAS. In the present study, the neuropsychological profiles of 21 adult males with HFASD were compared to 22 age and Performance IQ matched healthy control participants across six neuropsychological domains using independent samples t tests to determine whether individuals with HFASD exhibit a pattern of strengths and weaknesses that is consistent with CCAS. We found that the HFASD group performed worse than the control group within most domains of neuropsychological functioning. Significant differences were found on speeded motor tasks. Differences approached significance for one measure of attention and in two areas of executive functioning, but did not reach significance after adjusting for multiple comparisons.

Individuals with HFASD showed patterns of neuropsychological weakness that were consistent with some areas of research, particularly in motor functioning. The HFASD group performed significantly worse than the control group on a task of motor speed; this is consistent with other research that has found impairments in motor functioning of individuals with ASD (Freitag et al., 2006; Sachse et al., 2013; Tsatsanis, 2014). This difference in motor speed has clear connections to other areas of research that implicate cerebellar dysfunction in ASD.

No differences were found between the HFASD and control groups in receptive or expressive language; however, this difference is not unforeseen due to the similarity between the groups on verbal IQ. There is some inconsistency and inconclusiveness in regards to attention differences in individuals with HFASD compared to controls

(Tsatsanis, 2014). Inconsistent results were maintained within this study; the HFASD group had variable performance compared to the control group, but differences were not significant.

Some findings were inconsistent with other lines of research, especially in the areas of memory and executive functioning. Specifically, no differences were found between the control and HFASD groups in the domain of memory. This is surprising due to research suggesting deficits in spatial working memory, episodic memory, and retrieval (Tsatsanis, 2014). Finally, differences in executive functioning for individuals with ASD, particularly in the areas of cognitive flexibility and planning, are a common finding within the literature (Tsatsanis, 2014). The most unexpected result of this study is that while the HFASD group performed worse than the control group across all tasks of executive functioning, none of the tests were significantly different after adjusting for multiple comparisons.

In this study, we did not find the patterns of strengths and weaknesses consistent with CCAS in the group of individuals with HFASD; however, this does not preclude the involvement of the cerebellum in HFASD. In fact, differences between the HFASD and control groups on the motor speed tasks further supports the literature suggesting cerebellar involvement in ASD (Allen et al., 2004). Additionally, CCAS is a collective pattern of deficits, but not all individuals with cerebellar damage exhibit all of the distinct features of CCAS (Omar et al., 2014). Therefore, when examined at a group level, the features of CCAS may have been obscured in this sample of individuals with HFASD. Furthermore, perhaps differences in cerebellar anatomy or the functional connectivity of the cerebellum after distinct cerebellar insult is different than the developmentally acquired cerebellar differences in individuals with ASD.

The heterogeneity of ASD has been a growing area of attention in the field of autism research. Distinct patterns of deficits may not be found across a heterogeneous sample of

individuals with HFASD. Some researchers suggest that instead of examining group differences between individuals with ASD and control groups, which introduces the “averaging artifact,” investigators should instead use a multiple case series approach to examine individual neuropsychological profiles (Towgood, Meuwese, Gilbert, Turner, & Burgess, 2009). Therefore, future research should examine the individual neuropsychological profiles of individuals with HFASD to determine whether they exhibit the pattern of strengths and weaknesses consistent with CCAS.

Finally, while examining the neuropsychological profiles of individuals with HFASD can give us unique insight into the neurobehavioral aspects of HFASD, this research would be incomplete without connecting differences in neurocognitive functioning with imaging research. Perhaps because ASD is a heterogeneous neurodevelopmental disorder, the cerebellar anatomy or the functional connectivity of the cerebellum with other areas of the brain may develop differently for each individual with ASD. Future studies should combine a multiple case series approach with fMRI data to examine whether differences in the functional connectivity of the cerebellum with other areas of the brain can predict the pattern of strengths and weaknesses seen in individual neuropsychological profiles.

This study focuses on a restricted sample of individuals with HFASD, which limits the generalizability of its findings to young adult males with HFASD and high average IQ. ASD is more prevalent in males and boys are 4.5 times more likely to be diagnosed with autism than girls; however, future research should examine whether these findings can be generalized to females with HFASD (Baio, 2014). Additionally, this study examined individuals with very high intelligence. Intelligence does have an impact on neuropsychological functioning and results should be interpreted with caution when generalizing to individuals across a range of cognitive abilities (Rommelse et al., 2015).

Developmental concerns must also be raised. Anatomical differences in the cerebellum in younger children and potential changes in functional connectivity may impact the neuropsychological functioning of individuals across their lifespan. Future research should not only use cross-sectional methods, but should examine the neuropsychological functioning of individuals with ASD longitudinally. Another limitation of this study is its relatively small sample size, which has implications for the power of this study to detect differences. This study should be replicated utilizing a larger sample size so more robust conclusions about the differences in neuropsychological findings can be made.

The cerebellum has an important role in the neuropsychological functioning of individuals with HFASD, but future studies should utilize neuroimaging techniques to determine whether differences in cerebellar anatomy or functional connectivity can predict deficits seen within the neuropsychological profile of individuals of HFASD. Furthermore, it should be determined whether differences in functional connectivity can explain the heterogeneity of the neuropsychological profiles of ASD. Utilizing a combination of neuropsychological measures and neuroimaging will provide the greatest evidence regarding whether individuals with HFASD have cerebellar cognitive affective syndrome.

## **Appendix A: Neuropsychological Assessment Psychometric Information**

### **Boston Naming Test-2**

The Boston Naming Test-2 (BNT; Kaplan et al., 2001) is a visual naming ability test. Internal consistency (coefficient alpha) is between .78 and .96; test-retest reliability estimates vary depending on the population and time interval (.59-.91); it correlates highly with other language measures (Visual Naming Test of the Multilingual Aphasia Examination [ $r=.76$ - to  $.86$ ]) and with verbal measures of intelligence ( $r=.61$ ) (Strauss et al., 2006).

### **Brief Visuospatial Memory Test-Revised**

The Brief Visuospatial Memory Test-Revised (BVM-T-R; Benedict, 1997) assesses visual memory. Test-retest reliability for total recall is high (.80); interrater reliability is high ( $>.90$ ); it correlates strongly with measures of explicit memory ( $r=.65$ -.80) and with measures of visuospatial construction ( $r=.65$ -.66) (Strauss et al., 2006).

### **Conner's Continuous Performance Test, Second Edition**

The Conner's Continuous Performance Test, Second Edition (CPT-II; Conners & MHS Staff, 2000) is a measure of sustained attention. Internal consistency is very high for omission errors ( $r=.94$ ); test-retest stability is high for omission errors ( $r=.80$  to  $.89$ ); in factor analysis, omission errors emerged as a factor of inattention (Strauss et al., 2006).

### **Digit Span Forward**

The Digit Span Forward subtest from the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV; Wechsler, 2008) is a measure of elementary attention. Split-half reliability of Digit Span is very high (.93); test-retest reliability of digit span is high (.83) (Wechsler, 2008).



### **Hopkins Verbal Learning Test-Revised**

The Hopkins Verbal Learning Test-Revised (HVLT-R; Brandt & Benedict, 2001) is a measure of verbal memory. Test-retest reliability for Total Recall is moderately high (.74); it shows convergent validity with similar tests (e.g., CVLT); it correlates more strongly with verbal memory (e.g. WMS-R Logical Memory [ $r = .65$  to  $.77$ ]) than visual memory (e.g. WMS-R Visual Reproduction [ $r = .54$  to  $.69$ ]) (Strauss et al., 2006).

### **Judgment of Line Orientation**

The Judgment of Line Orientation (JLO; Benton et al., 1994) test is a measure of spatial perception. Split-half reliability is high (.84 to .91); test-retest reliability is very high (.90); it correlates more strongly with visual spatial subtests (e.g. WAIS-R Block Design [ $r = .68$ ] and Object Assembly [ $r = .69$ ]) than with verbal subtests (e.g. WAIS-R Information [ $r = .45$ ] and Vocabulary [ $r = .28$ ]) (Strauss et al., 2006).

### **Lafayette Grooved Pegboard**

The Lafayette Grooved Pegboard (Matthews & Klove, 1964) is a test of motor speed. Test-retest reliability is high (.67 to .86); pegboard time is moderately related to tapping speed ( $r = -.35$ ) (Strauss et al., 2006).

### **Peabody Picture Vocabulary Test, Fourth Edition**

The Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4; Dunn & Dunn, 2007) is a measure of receptive language. Internal consistency is very high with split-half reliability (.90-.97) and alpha coefficient (.93 to .98); it correlates well with measures of oral language and expressive vocabulary (Dunn & Dunn, 2007).

### **Trails B**

The Trail Making Test (TMT; Strauss et al., 2006) Trails B is a measure of mental flexibility. Test-retest reliability is adequate for Trails B (.75); interrater reliability is high (.90).

**Verbal Fluency**

Verbal Fluency (Strauss et al., 2006) is assessed through measures of phonemic and semantic fluency. Coefficient alpha for phonemic fluency is high ( $r=.83$ ); test-retest correlations are high for phonemic and semantic fluency ( $>.70$ ); semantic and phonemic fluency are moderately correlated with each other ( $.34-.64$ ) (Strauss et al., 2006).

**Wechsler Abbreviated Scale of Intelligence**

The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) is a brief measure of intelligence. Internal consistency is high, with high split-half reliability across subtests ( $.8$  to  $.9$ ); test-retest reliability is high ( $.88$ ); interscorer agreement is high ( $>.9$ ); correlations with the WAIS-III were high for both Performance IQ ( $.84$ ) and Verbal IQ ( $.88$ ) (Strauss et al., 2006).

**Wisconsin Card Sorting Test**

The Wisconsin Card Sorting Test (WCST; Heaton & PAR Staff, 2003) measures executive functions. Test-retest reliability for individuals with ASD is high ( $>.90$ ); factor analysis reveals three factors (the ability to shift set, problem solving/hypothesis testing, and response maintenance) (Strauss et al., 2006).

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